

**EXAMINER'S AMENDMENT**

1. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on 3/19/09, Mr. Yong Lu requested an extension of time for 2 MONTH(S) and authorized the Director to charge Deposit Account No. 50-1283 the required fee of \$245.00 (small entity fee) for this extension.

Furthermore, during the same telephone conversation conducted on 3/19/09, Mr. Yong Lu requested an amendment to change two dependent claims into two independent claims. The total number of independent claims in the application to be allowed will be four independent claims. Thus, Mr. Yong Lu authorized the Director to charge Deposit Account No. 50-1283 the required fee of \$110.00 (small entity fee) for these additional independent claims, and authorized the following examiner's amendment.

Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. The application has been amended as follows:

Claim 58, has been amended as follows:

Claim 58 (currently amended). An optical labeling molecule for labeling a target analyte comprising:

- a. a boron difluoride diaza-indacene-propionic acid (BODIPY) zwitterionic dye moiety comprising at least one positive or at least one negative charge moiety added to obtain a net neutral charge, wherein the positive charge moiety is selected from a group consisting of a quaternary ammonium group and a guanidinium group, wherein the positive charge moiety is not titratable between the pH of 3-12, and wherein the negative charge moiety is selected from the group consisting of a sulfonate group and a sulfate group, wherein the negative charge moiety is not titratable between the pH of 3-12;
- b. a functional linker moiety; and
- c. a titratable group moiety, wherein the titratable group is a tertiary amine which closely approximates the pK of the group removed from the target analyte by reaction with the functional linker.

Claim 65 has been amended as follows:

Claim 65. The optical labeling molecule of claim [65] 64, wherein the photocleavable moiety is selected from a group consisting of an O-nitrobenzylic compound, a benzoin moiety, and a nitrophenylcarbamate ester.

Claim 69, has been amended as follows:

Claim 69. The optical labeling molecule of claim 58, wherein the dye moiety [comprises boron difluoride diaza-indacene-propionic acid (BODIPY)] further comprising at least one added negative charge moiety selected from a sulfonate group or a sulfate group

and at least one added positive charge moiety selected from a group consisting of a quaternary ammonium group, a guanidinium group and a positive charge group.

Claim 75, has been amended as follows:

Claim 75. The optical labeling molecule of claim 58 comprising:

- [(a) a difluoride diaza-indacene-propionic acid (BODIPY) dye moiety, having at least one quaternary ammonium group and at least one sulfonate group, wherein said charged moieties are non-titratable between the pH of 3-12;
- (b) a titratable group moiety wherein the said titratable group is a tertiary amine;
- and
- (c)] a functional linker moiety wherein such linker is a N-hydroxysuccinimidyl ester.

In claim 77, line 1, "of claim 58" has been deleted.

In claim 78, "of claim 58" has been deleted.

As to claim 82, please include the underlined claim language as follows,

Claim 82. The optical labeling molecule of claim 58, prepared by

- (a) providing a boron difluoride diaza-indacene-propionic acid (BODIPY) dye moiety comprising one or more positive or one or more negative charge moieties;
- (b) adding at least one positive charge moiety selected from the group consisting of a

quaternary ammonium group, a guanidinium group and a positive charge group, wherein the positive charge moiety is not titratable between the pH of 3-12, or at least one negative charge moiety selected from a group consisting of a sulfonate group and a sulfate group, wherein the negative charge group is not titratable between the pH of 3-12 to form a zwitterionic dye moiety;

(c) contacting the zwitterionic dye moiety with a titratable group moiety; and

(d) contacting the product from step (c) with a functional linker moiety to provide a optical labeling molecule comprising a zwitterionic dye moiety characterized by a net neutral charge when bound to the target analyte.

***Allowable Subject Matter***

3. Claims 58-60 and 62-83 are allowed.

4. The following is an examiner's statement of reasons for allowance: the prior art of record (Haugland) fails to teach or fairly suggest having a boron difluoride diaza-indacene-propionic acid (BODIPY) zwitterionic dye moiety because Haugland's BODIPY dye moiety has uncharged canonical representations. Furthermore, the prior art of record fails to teach or fairly suggest having a dye moiety comprising a negative charge moiety selected from the group consisting of one or more sulfonate groups and sulfate groups that is not titratable between the pH of 3-12; having a titratable group moiety that is a tertiary amine and closely approximates the pK of the group removed from the target analyte by reaction with the functional linker; having two quaternary ammonium groups, or one or more guanidinium groups; having the general structures,

i.e., T-ZD-A-, ZD-T-A-, or T-ZD-C-I-A-, since Haugland does not disclose a tertiary amine (T); and the optical labeling molecules recited in claims 24 and 25, in combination with the remaining features and elements of the claimed invention.

In the examiner's opinion, it would not have been obvious to a person of ordinary skill in the art to modify Haugland's dye molecule by conjugating a tertiary amine to his molecule since Haugland does not disclose any suggestion that the disclosed molecules need to be modified, by adding a tertiary amine, for the intended purpose of his invention or for other scientific applications.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Conclusion***

5. The following prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Fung et al., and Panchuk-Voloshina et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LORE RAMILLANO whose telephone number is (571)272-7420. The examiner can normally be reached on Mon. to Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jill Warden/  
Supervisory Patent Examiner, Art Unit 1797

Lore Ramillano  
Examiner  
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3/26/09